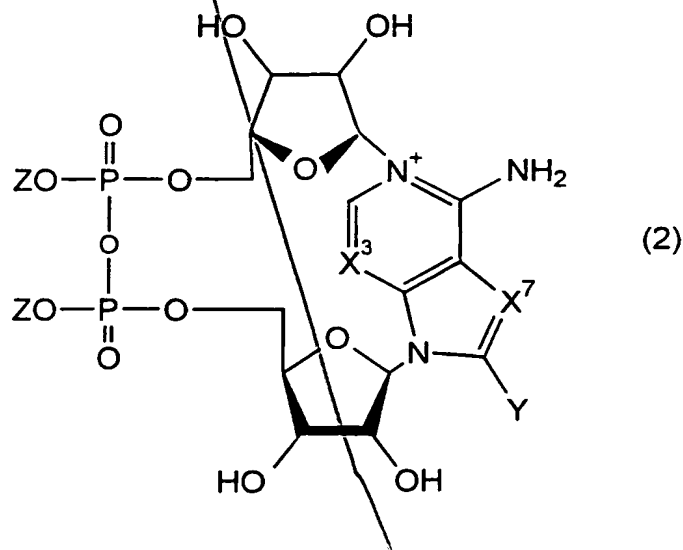


CLAIMS

- Sub 92
1. Use of a compound capable of antagonising a sustained cADPR-mediated rise in intracellular Ca^{2+} levels in a T cell, said rise being in response to stimulation of the T cell receptor/CD3 complex of the T cell, in the manufacture of a medicament for use in modulating T cell activity.
 2. Use according to claim 1 wherein the compound modulates the binding of cADPR to a ryanodine receptor/ Ca^{2+} channel.
 3. Use according to claim 1 or claim 2 wherein the compound is a cADPR analogue.
 4. Use according to claim 3 wherein the compound comprises an adenine component to which is individually linked two ribose moities or a derivative(s) thereof, which ribose moities are joined via a pyrophosphate bridging group.
 5. Use according to claim 3 wherein the compound has the formula (2):



Sub A2
wherein:

X³ is independently selected from CR¹ and N;

X⁷ is independently selected from CR² and N;

Y is halo, C₁ to C₂₀ hydrocarbyl, N(R³)(R⁴), OR⁵, SR⁶ nitro and carboxyl;

each of R¹, R², R³, R⁴, R⁵ and R⁶ is independently selected from H and C₁ to C₂₀ hydrocarbyl; and

Z is independently selected selected from H and a caging group;

or a bio-isostere; or a pharmaceutically acceptable salt thereof.

6. Use of a compound as defined in any one of claims 1 to 5 in the manufacture of a medicament for use in modulating the immune response of a mammal.

7. Use of a compound as defined in any one of claims 1 to 5 in the manufacture of a medicament for use in treating an autoimmune disease or graft rejection.

Sub A3
8. Use according to claim 7 wherein the autoimmune disease is selected from thyroiditis, insulinitis, multiple sclerosis, iridocyclitis, uveitis, orchitis, hepatitis, Addison's disease, myasthenia gravis, rheumatoid arthritis and lupus erythematosus.

9. Use of a compound as defined in any one of claims 1 to 5 in the manufacture of a medicament for use in treating or preventing an immune disorder in a human or animal.

10. A method of treating a human or animal patient suffering from an immune disorder which method comprises administering to the patient an effective amount of a compound as defined in any one of claims 1 to 5.

11. A method for identifying a substance capable of modulating a sustained rise in Ca²⁺ entry via a cADPR-mediated pathway which method comprises:

(i) contacting an ADP-ribosyl cyclase or a homologue, variant or derivative thereof, with a substance to be tested under conditions that would permit the synthesis of cADPR in the absence of the substance; and

(ii) determining whether the substance affects cADPR synthesis.

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12. A method according to claim 11 wherein the substance inhibits cADPR synthesis.
13. A method for identifying a substance capable of modulating a sustained rise in Ca^{2+} entry *via* a cADPR-mediated pathway which method comprises:
- (i) contacting a T cell, which has been stimulated *via* its T cell receptor, with a candidate substance under conditions that would permit a sustained rise in intracellular Ca^{2+} levels in the absence of the substance; and
 - (ii) determining whether the substance inhibits a sustained rise in intracellular Ca^{2+} levels.
14. A compound identified by the method of claim 11, 12 or 13 for use in treating or preventing an immune disorder.
- Sub A* 15. A compound identified by the method of claim 11, 12 or 13.
16. A process comprising the steps of:
- (a) performing the method according to claim 11, 12 or 13;
 - (b) preparing a quantity of those one or more substances identified as being capable of modulating a sustained rise in Ca^{2+} entry *via* a cADPR-mediated pathway.
17. A process comprising the steps of:
- (a) performing the method according to claim 11, 12 or 13; and
 - (b) preparing pharmaceutical composition comprising one or more substances identified as being capable of modulating a sustained rise in Ca^{2+} entry *via* a cADPR-mediated pathway.
18. A process comprising the steps of:
- (a) performing the method according to claim 11, 12 or 13; and
 - (b) modifying one or more of the substances identified as being capable of modulating a sustained rise in Ca^{2+} entry *via* a cADPR-mediated pathway to cause a different effect on T cell activity.
- Sub A*